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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,145	11/05/2001	Bruce L. Roberts	GA0201C	2591

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,145	ROBERTS, BRUCE L.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-20* is/are pending in the application.

4a) Of the above claim(s) *1,4-6,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,7,9,10 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/05 has been entered.

Claim 8 was canceled as requested.

Claims 1-7 and 9-20 remain pending in the application.

Claims 1, 4-6, 11, and 12 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. See previous Action of 11/17/04. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/1/03.

Claims 2, 3, 7, 9, 10, and 13-20 are under consideration in this Office Action.

Drawings

No drawings are on file in the instant application.

Priority

Applicant's amendment to the specification is sufficient to obtain priority to PCT/US99/13800, filed 6/18/99.

Rejections Withdrawn

The rejection of claims 7, 9, and 10 under 35 U.S.C. 102(b) as being anticipated by Hieshima (1997) is withdrawn in view of Applicant's amendment requiring that the polynucleotide must encode a tumor-associated antigen.

The rejection of claims 2, 3, 7, 9, 10, and 13-20 under 35 USC 103 over Glenn in view of Staats is withdrawn in favor of new rejections under 35 USC 103 that better address the instant claims.

Claim Objections

Claims 2, 3, 7, 9, 10, and 13-20 stand objected to because they recite non-elected subject matter, i.e. TARC, MCP-4, MDC, ecalectin, MCP-2, and eotaxin 3.

Claim 16 is objected to because it does not further limit claim 7, which already requires the presence of a polynucleotide encoding a tumor antigen.

Withdrawn claims 4-6 are objected to because the amendment presents them using incorrect status identifiers. These claims are identified as "(Original)", instead of "(Withdrawn)". See 37 CFR 1.121(c).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17 and 18 are currently drawn to compositions comprising two separate polynucleotide molecules, one molecule encoding a tumor antigen and PARC, and the second separate molecule encoding a tumor-associated antigen. These claims can be interpreted as embracing compositions comprising one plasmid molecule encoding PARC and a first tumor antigen, and a second plasmid molecule encoding a second tumor antigen. In a broader interpretation, a composition comprising two identical copies of a plasmid molecule encoding PARC and a first tumor antigen would satisfy the claim.

Applicant states that support for amendments is found at paragraphs 58 and 228 of the specification. However, these passages do not support the embodiment in which the claimed composition comprises one plasmid molecule encoding PARC and a first tumor antigen, and a second plasmid molecule encoding a second tumor antigen. A review of the specification shows that there is support for a single polynucleotide molecule encoding PARC and a tumor antigen, as well as for a composition comprising separate polynucleotide molecules wherein one encodes PARC and the other encodes a tumor antigen. However, there is no readily apparent support for a composition

comprising both a molecule encoding PARC and a first tumor antigen and a separate molecule encoding a second tumor antigen. For these reasons claims 17 and 18 introduce new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 3, 7, 9, 10, and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staats et al (US Patent 6,270,758, issued 8/7/01) in view of Carson et al (US Patent 5,679,647, issued 10/21/97) and Glenn et al (US Patent 5,980,898, issued 11/9/99).

Staats taught methods method of eliciting an immune response against an antigen in a vertebrate subject comprising the steps of providing an antigen-adjuvant composition comprising the antigen and a substantially non-toxic adjuvant molecule having biological activity in mucosal tissues, and administering said antigen-adjuvant composition to the vertebrate subject in a manner such that initial contact occurs in mucosal tissue of the vertebrate subject, whereby an immune response is elicited. Cytokines are preferred adjuvants. PARC is a suggested adjuvant. See abstract, column 10, lines 10-15; and column 7, lines 29-31. Staats taught that PARC and tumor antigens could be produced recombinantly from expression vectors.

Staats did not teach a single polynucleotide encoding both PARC and a tumor antigen, a composition comprising separate polynucleotide molecules, one encoding PARC and the other encoding a tumor antigen, or a composition comprising both a first polynucleotide that can express PARC and a tumor antigen, and a second separate polynucleotide encoding a tumor antigen.

Carson taught a method for stimulating cytotoxic T lymphocytes reactive with tumor-associated antigen present on tumor cells in a mammalian host, comprising administering to the mucosa of a host a polynucleotide encoding a tumor antigen. Carson further taught coimmunization with a several different polynucleotides encoding a variety of different tumor-associated antigens (see claim 8), and coadministration of polynucleotides encoding cytokines (see claim 10).

Glenn taught methods of immunization in which a tumor-associated antigen is delivered with a chemokine adjuvant. See abstract; column 9, lines 34-46; column 3, lines 66 and 67; and claim 1 at column 34. Both the antigen and the adjuvant may be encoded by a polynucleotide, and the polynucleotide may comprise expression control sequences including promoters, enhancers, silencers, splice sites, polyadenylation signals, and an internal ribosome entry site (IRES). See column 4, lines 24-27, and column 14, lines, 13-23. Glenn also taught the use of delivery vehicles including non-integrating nucleic acids and transfection-promoting agents such as cationic lipids. See column 14, lines 16-27.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Staats by making and administering a nucleic acid

vaccine comprising expression vectors encoding the tumor antigen and PARC of Staats. Because Carson taught that polypeptide vaccines suffer from several drawbacks including the risk of potential toxicities, particularly at dosages sufficient to produce a biological response to the peptide, the cost associated with isolating and purifying or synthesizing the peptides, and their relatively short half-life in vivo which usually results from their degradation by any proteases present in the target tissue. See column 1, lines 35-46. In contrast, and that nucleic acid vaccines are more stable, are not subject to proteolysis prior to entering a cell, and are easier and less expensive to prepare than protein-based vaccines. Also, Carson taught that injection of protein (e.g., in a vaccination scheme) does not usually induce cytotoxic T cell formation because exogenous proteins do not efficiently enter the class I processing pathway, whereas polynucleotide vaccines do stimulate CTL formation. See column 2, lines 48-51.

The organization of the nucleic acid(s) encoding the tumor antigen and adjuvant (PARC) of Staats is a matter of design choice. For example, pertinent to instant claim 3, one of ordinary skill in the art aware of the teachings of Glenn would have recognized that the suggested use of an IRES would allow linkage of antigen and adjuvant open reading frames under control of a single promoter, allowing coordinate expression of these proteins. On the other hand, pertinent to claims 2 and 13, the open reading frames could be placed under the control of promoters of different strengths on the same vector in order to adjust the relative amounts of antigen and adjuvant expressed. Alternatively, pertinent to claim 14, one could place the antigen and adjuvant open reading frames under the control of different promoters on different expression vectors,

and adjust the amount of expression of each protein by selecting an appropriate promoter and also adjusting the amount of expression vector delivered. Each of these approaches would allow one of ordinary skill in the art to control the amount of adjuvant and antigen expressed, and would have been obvious in view of the teachings of the cited art in view of the level of ordinary skill in the art.

Regarding claims 10 and 20, the target cells transfected by the method of Carson, would be considered to be the claimed host cells. With regard to claim limitations requiring that PARC must be secreted, this is considered to be an inherent property of PARC, and chemokines in general, such that one of ordinary skill in the art following the teachings of Staats and Malone would use a nucleic acid encoding a secreted form of PARC.

Claims 17 and 18 require a composition comprising a polynucleotide that can express PARC and a tumor antigen, and a second separate polynucleotide encoding a tumor antigen. These claims can be broadly interpreted as being drawn to compositions comprising more than one polynucleotide that can express PARC and a tumor antigen. To the extent that these claims read on this interpretation, they are obvious in view of the cited references because one of ordinary skill in the art would be in possession of such a composition immediately upon performing a standard plasmid preparation. That is, the process of isolating and purifying a polynucleotide results in a composition comprising millions of copies of the polynucleotide.

On the other hand, It would have been obvious to one of ordinary skill in the art at the time of the invention to make and administer a composition comprising a

polynucleotide that can express PARC and a first tumor antigen, and a second separate polynucleotide encoding a second tumor antigen. One would have been motivated to do so because Carson taught that one obstacle to cancer immunotherapy based on immunization of the host to tumor associated antigens is tolerance by the host immune system to such antigens, but that T lymphocyte immune tolerance to a self-antigen can be broken by immunizing the host with a mixture of self-antigens and foreign molecular mimics of such antigens. See column 4, lines 43-49, and claim 8.

Response to Arguments

Applicant's arguments filed 5/19/05 have been fully considered as they might apply to the new ground of rejection above but they are not persuasive.

Applicant argued at pages 3 and 4 of the response that, essentially, the Office improperly considered PARC to be an art-recognized equivalent of the chemokines set forth in Glenn. This argument is moot in view of the new grounds of rejection above that does not depend upon equivalence of the chemokines of Glenn with PARC.

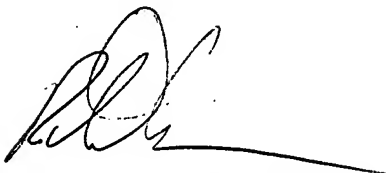
Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the

hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.



Richard Schnizer, Ph.D.